Applicant: Van Beusechem Application No. 10/501,407 Filing Date: March 25, 2005 Docket No.: 294-293 PCT/US

Page 2

Please cancel claim 1;

Please add new claim 26;

Please amend claims 2-5, 9, 11, and 14 as follows:

## The following is a listing the pending claims:

- 1. Cancelled
- 2. (Presently amended) The recombinant virus according to claim 4 <u>26</u>, wherein the virus is a human adenovirus.
- 3. (Presently amended) The recombinant virus according to claim 4 26, wherein expression of at least one essential early adenovirus gene is controlled by a tumor-specific promoter.
- 4. (Presently amended) The recombinant virus according to claim ± 26, wherein the adenovirus is a heterologously trans-complemented adenovirus.

Applicant: Van Beusechem Application No. 10/501,407 Filing Date: March 25, 2005 Docket No.: 294-293 PCT/US

Page 3

5. (Presently amended) The recombinant virus according to claim 4 26, wherein the virus genome comprises at least the gene encoding the adenovirus E1B-19kDa protein or a functional analog or derivative thereof.

- 6. (Previously presented) The recombinant virus according to claim 5, wherein the virus genome further comprises the gene encoding the adenovirus E1B-19kDa protein or a functional analog or derivative thereof.
- 7. (Previously presented) The recombinant virus according to claim 5, wherein the virus genome comprises one or more of the genes of the adenovirus E4 region encoding E4 proteins or functional analogues or derivatives thereof.
- 8. (Previously presented) The recombinant virus according to claim 7, wherein the virus genome comprises at least the gene encoding the adenovirus E4 or F6 protein or functional analogues or derivatives thereof.
- 9. (Presently amended) The recombinant virus according to claim 4 26, wherein the adenovirus carries a mutation in a E1A region encompassing at least part of the pRb-binding CR2 domain of E1A.

Applicant: Van Beusechem Application No. 10/501,407 Filing Date: March 25, 2005

Docket No.: 294-293 PCT/US Page 4

- 10. (Withdrawn) The recombinant virus according to claim 1, wherein the restoring factor is chosen from the group consisting of p53, p63, p73, BAX, BAK, BOK/Mtd, BCL-Xs, Noxa/APR, PIDD, p53AIP1, PUMA, KILLER/DR5, Apaf-1, PIG, BID, tBID, BAD, HRK, Bik/Nbk, BLK, mda-7, p14ARF or functional variants, analogues or derivatives thereof.
- 11. (Presently amended) The recombinant virus according to claim 4 26, wherein the restoring factor is p53 protein or a functional analogue or derivative thereof.
- 12. The recombinant virus according to claim 11, (Previously presented) wherein the protein lacks a functional binding domain for a human MdM2 protein.
- 13. (Previously presented) The recombinant virus according to claim 11, wherein the protein is a functional derivative of human p53 with mutated amino acids Leu-14 and Phe-19.
- (Presently amended Previously presented) The recombinant virus according to 14. claim + 26, wherein the target cell is a human cell chosen from the group consisting of cancer cells, arthritic cells, hyperproliferative vascular smooth muscle cells and cells infected with a virus other than said recombinant virus.

Applicant: Van Beusechem Application No. 10/501,407

Filing Date: March 25, 2005 Docket No.: 294-293 PCT/US

Page 5

15. (Withdrawn) Use of the recombinant virus according to claim 1 in a

medicament.

16. (Withdrawn) Use according to claim 15 for the manufacture of a medicament for

suppressing uncontrolled cell growth.

17. (Withdrawn) A method for lysing target cells hampered in the p53 dependent

apoptosis pathway, comprising the steps of:

-infecting the said target cells with the replication competent recombinant virus

according to claim 1, and

-replicating said virus within said target cells, further comprising the step of

providing, in the virus genome, the coding sequence of at least one restoring factor functional in

restoring the p53 dependent apoptosis pathway, said coding sequence being capable to be

expressed in the target cells upon infection thereof by said virus.

18. Cancelled

19. (Withdrawn) The method according to claim 17, further comprising the step of

subjecting said target cells to at least one of irradiation and a toxic chemical compound.

Applicant: Van Beusechem Application No. 10/501,407 Filing Date: March 25, 2005 Docket No.: 294-293 PCT/US

Page 6

- 20. (Withdrawn) The method according to claim 17, wherein said target cells are present in an animal body.
- 21. (Withdrawn) A method for treatment of a subject body suffering from a condition involving body cells hampered in a p53 dependent apoptosis pathway, comprising the step of administering to said subject body an effective amount of the replication competent recombinant adenovirus according to claim 1.
- 22. (Withdrawn) The method according to claim 21, wherein the condition is associated with uncontrolled cell growth.
- 23. (Withdrawn) The method according to claim 22, wherein the condition is chosen from the group consisting of cancer, arthritis, and vascular smooth muscle cell hyperplasia.
- 24. (Previously presented) The recombinant virus according to claim 2, wherein the human adenovirus comprises serotype 5.
- 25. (Previously presented) The recombinant virus according to claim 9, wherein the mutation comprises a deletion encompassing amino acids 122-129 (LTCHEAGF) (SEQ. ID. %) of E1A.

Applicant: Van Beusechem Application No. 10/501,407 Filing Date: March 25, 2005

Docket No.: 294-293 PCT/US

Page 7

26. (New) A replication competent recombinant adenovirus, being capable to replicate and having lytic capacity in target cells, wherein said target cells are hampered in a p53 dependent apoptosis pathway, wherein the adenovirus is a conditionally replicating adenovirus; wherein the adenovirus genome comprises a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway in said target cells; wherein said coding sequence is operably linked to one or more expression control sequences functional in said target cells, and whereby said restoring factor induces accelerated cell lysis and/or a faster release of virus progeny when compared to a recombinant adenovirus lacking said coding sequence.